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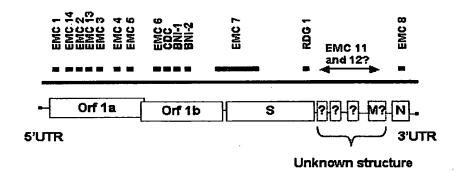
- (74) Agent: WINCKELS, J., H., F.; Nieuwe Parklaan 97, NL-2587 BN Den Haag (NL).
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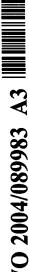
- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SEVERE ACUTE RESPIRATORY SYNDROME (SARS) CAUSING CORONAVIRUS



(57) Abstract: The invention relates to the field of virology. The invention provides an isolated essentially mammalian positive-sense single stranded RNA virus (SARS) within the group of coronaviuses and components thereof. The effect of pegylated interferon-alpha on SARS infection has been analysed.



•	INTERNATIONAL SEARCH REPORT	ational Application No /NL2004/000229
A. CLASSII IPC 7	CO7K14/165 C12N15/85 C12N5/10 C07K16/ G01N33/569 A61K39/215 A61K38/21 A61P31/	
According to	International Patent Classification (IPC) or to both national classification and IPC	
	SEARCHED	
	cumentation searched (classification system followed by classification symbols) A01K C07K C12N A61K	
Documentat	ion searched other than minimum documentation to the extent that such documents are inc	luded in the fields searched
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C. DOCUM	ENTS CONSIDERED TO BE RELEVANT	· · · · · · · · · ·
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	POUTANEN SUSAN M ET AL: "Identification of severe acute respiratory syndrome in Canada." NEW ENGLAND JOURNAL OF MEDICINE, vol. 348, no. 20, 31 March 2003 (2003-03-31), pages 1995-2005, XP002255633 ISSN: 0028-4793	1-27

X Further documents are listed in the continuation of box C.	Y Patent family members are listed in annex.
Special categories of cited documents: 'A' document defining the general state of the art which is not considered to be of particular relevance 'E' earlier document but published on or after the international filling date 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'O' document referring to an oral disclosure, use, exhibition or other means 'P' document published prior to the international filing date but later than the priority date claimed	 "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search 27 October 2004	Date of mailing of the international search report 25/11/2004
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Brouns, G

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'/NL2004/000229

DOCUMENTS CONSIDERED TO BE RELEVANT				
C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Category Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.				
tion of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
CENTERS FOR DISEASE CONTROL AND PREVENTION: "Update: Outbreak of severe acute respiratory syndrome: Worldwide, 2003." MORBIDITY AND MORTALITY WEEKLY REPORT, vol. 52, no. 12, 28 March 2003 (2003-03-28), pages 241-248, XP002288825 ISSN: 0149-2195 page 243, paragraph 2	1-27			
DATABASE EMBL E.B.I. HINXTON, UK; 15 April 2003 (2003-04-15), S. JONES: "SARS Coronavirus TOR2, complete genome" XP002288827 retrieved from EMBL Database accession no. AY274119 EMC-1=nts 2064-2932;2=4820-5166;3=8480-8928;4=9954-10633;5=nts12194-13525;6=nts 13877-14648;7=nts 20665-23772;8=nts 28228-28590;11=611-2091;12=4325-4770; 13=6338-7171;14=3579-4315;RDG1=24439-25090 abstract	1-27			
SNIJDER E J ET AL: "Unique and Conserved Features of Genome and Proteome of SARS-coronavirus, an Early Split-off From the Coronavirus Group 2 Lineage" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 331, no. 5, 29 August 2003 (2003-08-29), pages 991-1004, XP004447471 ISSN: 0022-2836 the whole document	1-27			
PEIRIS J ET AL: "Coronavirus as a possible cause of severe acute respiratory syndrome" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 361, no. 9366, 8 April 2003 (2003-04-08), pages 1319-1325, XP004421148 ISSN: 0140-6736 the whole document -/	1-27			
	CENTERS FOR DISEASE CONTROL AND PREVENTION: "Update: Outbreak of severe acute respiratory syndrome: Worldwide, 2003." MORBIDITY AND MORTALITY WEEKLY REPORT, vol. 52, no. 12, 28 March 2003 (2003-03-28), pages 241-248, XP002288825 ISSN: 0149-2195 page 243, paragraph 2 DATABASE EMBL E.B.I. HINXTON, UK; 15 April 2003 (2003-04-15), S. JONES: "SARS Coronavirus TOR2, complete genome" XP002288827 retrieved from EMBL Database accession no. AY274119 EMC-1=nts 2064-2932;2=4820-5166;3=8480-8928;4=9954-10633;5=nts12194-13525;6=nts 13877-14648;7=nts 20665-23772;8=nts 28228-28590;11=611-2091;12=4325-4770; 13=6338-717;14=3579-4315;RDG1=24439-25090 abstract SNIJDER E J ET AL: "Unique and Conserved Features of Genome and Proteome of SARS-coronavirus, an Early Split-off From the Coronavirus Group 2 Lineage" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 331, no. 5, 29 August 2003 (2003-08-29), pages 991-1004, XP004447471 ISSN: 0022-2836 the whole document PEIRIS J ET AL: "Coronavirus as a possible cause of severe acute respiratory syndrome" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 361, no. 9366, 8 April 2003 (2003-04-08), pages 1319-1325, XP004421148 ISSN: 0140-6736 the whole document			

iational Application No /NL2004/000229

		7NL2004/000229		
C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
A	GERBERDING JULIE LOUISE: "Faster but fast enough? Responding to the epidemic of severe acute respiratory syndrome." THE NEW ENGLAND JOURNAL OF MEDICINE. 15 MAY 2003, vol. 348, no. 20, 2 April 2003 (2003-04-02), pages 2030-2031, XP002288826 ISSN: 1533-4406 the whole document	1-27		
A	EP 0 278 541 A (DUPHAR INT RES) 17 August 1988 (1988-08-17) the whole document	1–27		
Α	WO 03/013599 A (AGRONOMIQUE INST NAT RECH; ENVT TOULOUSE (FR); GONON VALERIE (FR); AU) 20 February 2003 (2003-02-20) the whole document	1-27		
X	PEI JIANWU ET AL: "Chicken interferon type I inhibits infectious bronchitis virus replication and associated respiratory illness" JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, vol. 21, no. 12, December 2001 (2001-12), pages 1071-1077, XP002302419 ISSN: 1079-9907	28,29, 33,34, 36,40		
Y	abstract	30-32, 35, 37-39, 41,42		
X	SMITH A L ET AL: "INTRANASALLY ADMINISTERED ALPHA-BETA INTERFERON PREVENTS EXTENSION OF MOUSE HEPATITIS VIRUS STRAIN JHM INTO THE BRAINS OF BALB-CBYJ MICE" ANTIVIRAL RESEARCH, vol. 8, no. 5-6, 1987, pages 239-246, XP008037792 ISSN: 0166-3542	28,29, 33,36,40		
Y	page 242	30-32, 35, 37-39, 41,42		

ational Application No
/NL2004/000229

	/NL2004/000229			
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
TURNER R B ET AL: "PREVENTION OF EXPERIMENTAL CORONAVIRUS COLDS WITH INTRANASAL ALPHA-2B INTERFERON" JOURNAL OF INFECTIOUS DISEASES, vol. 154, no. 3, 1986, pages 443-447, XP008037795 ISSN: 0022-1899	28,29, 31, 33-35,40			
figure 1	30,32, 36-39, 41,42			
HAAGMANS BART L ET AL: "Pegylated interferon-alpha protects type 1 pneumocytes against SARS coronavirus infection in macaques." NATURE MEDICINE, vol. 10, no. 3, March 2004 (2004-03), pages 290-293, XP002302418 ISSN: 1078-8956 the whole document	28-42			
ANONYMOUS: "Viragen files patent application for drug to target SARS" INTERNET ARTICLE, 'Online! 2 June 2003 (2003-06-02), pages 1-2, XP002302417 Retrieved from the Internet: URL:http://www.amarbio.com/10News56.html>	28,29, 33,34, 40-42			
'retrieved on 2004-10-25! the whole document	30-32, 35-39			
STRÖHER UTE ET AL: "Severe acute respiratory syndrome-related coronavirus is inhibited by interferon- alpha." THE JOURNAL OF INFECTIOUS DISEASES. 1 APR 2004, vol. 189, no. 7, 1 April 2004 (2004-04-01), pages 1164-1167, XP008037651 ISSN: 0022-1899 the whole document	28,29, 31, 33-35, 37,40			
V KURIAN: "Can coconut drive SARS to nuts?" INTERNET ARTICLE, 'Online! 20 May 2003 (2003-05-20), page 1, XP002302422 Retrieved from the Internet: URL:http://www.blonnet.com/2003/05/20/stories/2003052000241700.htm> 'retrieved on 2004-10-25! paragraph '0004!	42			
	EXPERIMENTAL CORONAVIRUS COLDS WITH INTRANASAL ALPHA-2B INTERFERON" JOURNAL OF INFECTIOUS DISEASES, vol. 154, no. 3, 1986, pages 443-447, XPO08037795 ISSN: 0022-1899 figure 1 table 1 HAAGMANS BART L ET AL: "Pegylated interferon-alpha protects type 1 pneumocytes against SARS coronavirus infection in macaques." NATURE MEDICINE, vol. 10, no. 3, March 2004 (2004-03), pages 290-293, XPO02302418 ISSN: 1078-8956 the whole document ANONYMOUS: "Viragen files patent application for drug to target SARS" INTERNET ARTICLE, 'Online! 2 June 2003 (2003-06-02), pages 1-2, XP002302417 Retrieved from the Internet: URL:http://www.amarbio.com/10News56.html> 'retrieved on 2004-10-25! the whole document STRÖHER UTE ET AL: "Severe acute respiratory syndrome-related coronavirus is inhibited by interferon- alpha." THE JOURNAL OF INFECTIOUS DISEASES. 1 APR 2004, vol. 189, no. 7, 1 April 2004 (2004-04-01), pages 1164-1167, XPO08037651 ISSN: 0022-1899 the whole document V KURIAN: "Can coconut drive SARS to nuts?" INTERNET ARTICLE, 'Online! 20 May 2003 (2003-05-20), page 1, XP002302422 Retrieved from the Internet: URL:http://www.blonnet.com/2003/05/20/stor ies/2003052000241700.htm> 'retrieved on 2004-10-25!			

ational Application No
/NL2004/000229

		/NL2004/000229			
	(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
Α	MASCI PAUL ET AL: "New and modified interferon alfas: preclinical and clinical data." CURRENT ONCOLOGY REPORTS. MAR 2003, vol. 5, no. 2, March 2003 (2003-03), pages 108-113, XP008037765 ISSN: 1523-3790 the whole document	30-32			
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ternational application No. PCT/NL2004/000229

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 21, 22 and 40-42 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. X As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

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ational Application No /NL2004/000229

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 0278541	Α	17-08-1988	DK EP HU JP	13988 A 0278541 A1 45559 A2 63188390 A	17-07-1988 17-08-1988 28-07-1988 03-08-1988
WO 03013599	A	20-02-2003	FR EP WO	2828405 A1 1429803 A2 03013599 A2	14-02-2003 23-06-2004 20-02-2003